NATIONAL GUIDELINE CLEARINGHOUSE™ (NGC) GUIDELINE SYNTHESIS

SCREENING FOR CERVICAL CANCER

GUIDELINES BEING COMPARED

1. **American College of Obstetricians and Gynecologists (ACOG)**. Cervical cytology screening. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2009 Dec. 12 p. (ACOG practice bulletin; no. 109). [96 references]
2. **Kaiser Permanente Care Management Institute (KPCMI)**. Cervical cancer screening guideline: October 2006. Oakland (CA): Kaiser Permanente Care Management Institute; 2006 Oct. 124 p. [199 references]
3. **Program in Evidence-based Care (PEBC)**. Cervical screening. Toronto (ON): Cancer Care Ontario (CCO); 2005 May 20. 39 p. [74 references]

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AREAS OF AGREEMENT AND DIFFERENCE

A direct comparison of the recommendations presented in the above guidelines for screening for cervical cancer in average-risk, asymptomatic women is provided in the tables below. Recommendations for screening in women at increased risk of cervical cancer as well as recommendations for follow-up for abnormal cytology results are beyond the scope of this synthesis.

Areas of Agreement

Screening Modality

All three groups recommend both liquid-based and conventional cytology as appropriate methods of screening for asymptomatic, average-risk women. PEBC specifies LBP cytology as the preferred tool, but states that conventional smear

technology is an acceptable alternative. ACOG and KPCMI also cite co-testing using the combination of cytology plus HPV DNA testing as an appropriate screening test for women older than 30 years.

When to Discontinue Screening

Recommendations concerning when to stop screening are similar, with all three groups agreeing that screening can be discontinued in older women (between 65 and 70 years [ACOG]; age 65 [KPCMI]; age 70 [PEBC]) who have had at least three consecutive, normal Pap smears and no abnormal test results in the past ten years.

Screening after Hysterectomy

There is overall agreement that screening can be discontinued in women who have had a total hysterectomy for benign conditions and have no history of CIN (ACOG specifies high-grade CIN; KPCMI specifies CIN grade 2/3).

Areas of Difference

When to Initiate Screening

Recommendations regarding when to initiate cervical cancer screening differ, with ACOG recommending screening begin at age 21 years. They note that screening before age 21 should be avoided because it may lead to unnecessary and harmful evaluation and treatment in women at very low risk of cancer. KPCMI, in contrast, recommends initiation of cervical cancer screening approximately 3 years after first sexual intercourse or by the age of 21, whichever comes first. Lastly, PEBC recommends screening be initiated within three years of first vaginal sexual activity (i.e., vaginal intercourse, vaginal/oral, and/or vaginal/digital sexual activity), but does not specify an age by which screening should be initiated. PEBC chose not to include a specific age to initiate screening, citing lack of evidence to support a particular age over another. The guideline states that linking Pap testing to the initiation of vaginal sexual activity is also more practical than choosing a specific age.

While ACOG recommends against screening before the age of 21, they do recommend sexually active females younger than age 21 years be counseled and tested for sexually transmitted infections, and be counseled regarding safe sex and contraception, measures which may be carried out without cervical cytology.

Screening Interval

The organizations differ in their recommendations concerning the screening interval for asymptomatic, low- or average-risk women. PEBC is the only group to recommend annual screening, which they recommend be performed until there are three consecutive negative Pap tests, and thereafter every 2 to 3 years (every 3 years if screening is supported by an adequate recall mechanism). KPCMI recommends that all asymptomatic, average-risk women be screened every 3 years. They make no recommendation for or against routinely providing annual screening tests prior to beginning a triennial screening program. ACOG recommends biennial screening for women between the ages of 21 and 29 years,

and triennial screening for women aged 30 years and older who have had three consecutive negative cervical cytology screening test results and who have no history of CIN 2 or CIN 3, are not HIV infected, are not immunocompromised, and were not exposed to diethylstilbestrol in utero.

COMPARISON OF RECOMMENDATIONS	
WHOM TO SCREEN (INCLUDING WHEN TO INITIATE AND DISCONTINUE) Abbreviations Back to TOC	
ACOG (2009)	***The following recommendations are based on good and consistent scientific evidence (Level A)***: • Cervical cancer screening should begin at age 21 years. Screening before age 21 should be avoided because it may lead to unnecessary and harmful evaluation and treatment in women at very low risk of cancer. ***The following recommendations are based on limited and inconsistent scientific evidence (Level B)***: • Sexually active adolescents (i.e., females younger than age 21 years) should be counseled and tested for sexually transmitted infections, and should be counseled regarding safe sex and contraception. These measures may be carried out without cervical cytology and, in the asymptomatic patient, without the introduction of a speculum. • Because cervical cancer develops slowly and risk factors decrease with age, it is reasonable to discontinue cervical cancer screening between 65 years and 70 years of age in women who have three or more negative cytology test results in a row and no abnormal test results in the past 10 years. ***The following recommendations are based primarily on consensus and expert opinion (Level C)***: • Women who have been immunized against HPV-16 and HPV-18 should be screened by the same regimen as nonimmunized women. **NGC Note**: This synthesis addresses screening in asymptomatic women at average risk of cervical cancer. Discussion of recommendations related to screening in women at increased risk and recommendations related to follow-up for abnormal Pap smear results are beyond the scope of this synthesis. Refer to the original guideline document for additional recommendations on screening in women at increased risk of cervical cancer.

KPCMI (2006)	**Recommendations: Effectiveness of Cervical Cancer Primary Screening Tests in Asymptomatic, Average-Risk Women** Routine cervical cancer screening is recommended for all asymptomatic, average-risk women. ***(Evidence-based: B)*** **Recommendations: Optimal Age to Begin and End Screening in Asymptomatic, Average-risk Women** Initiation of cervical cancer screening is recommended approximately 3 years after first sexual intercourse or by the age of 21, whichever comes first.*† ***(Consensus-based)*** Routine screening for cervical cancer for women older than age 65 is not recommended if they have had adequate recent screening** with normal results on their last cytology (and HPV test if applicable). ***(Evidence-based: D)*** **The Guideline Development Team (GDT) recognizes that the age to begin screening may not adequately reflect the current The Health Plan Employer Data and Information Set (HEDIS) measures. Some regions may choose to offer screening at a younger age. The HEDIS®* cervical cancer screening rate estimates the percentage of women aged 21 to 64 that were enrolled in the health plan and who had one cytology test during measurement year or the two years prior.* *†Routine cervical cancer screening continues to be recommended for women who have received the HPV vaccine. For additional information, see Kaiser Permanente (KP) National HPV Vaccine Practice Resource.* ***The Guideline Development Team defined adequate recent screening as older women who have had three or more documented, consecutive, technically satisfactory normal/negative cervical cytology tests, and who have had no abnormal/positive cytology tests within the last 10 years.* **NGC Note**: This synthesis addresses screening in asymptomatic women at average risk of cervical cancer. Discussion of recommendations related to screening in women at increased risk and recommendations related to follow-up for abnormal Pap smear results are beyond the scope of this synthesis. Refer to the guideline summary for additional recommendations on the following topics: • Triage for ASC US Results Using HPV Testing in Asymptomatic, Average Risk Women • Screening in Women at Increased Risk of Cervical Cancer • Optimal Initial Management of Concurrent HPV Positive and Cytology Negative Cervical Screening Results

PEBC (2005)	**Screening Initiation** Cervical cytology screening should be initiated within three years of first vaginal sexual activity (i.e., vaginal intercourse, vaginal/oral, and/or vaginal/digital sexual activity) (C-III). **Screening Cessation** Screening may be discontinued after the age of 70 if there is an adequate negative screening history in the previous 10 years (i.e., 3 to 4 negative tests) (B-II). **NGC Note**: This synthesis addresses screening in asymptomatic women at average risk of cervical cancer. Discussion of recommendations related to screening in women at increased risk and recommendations related to follow-up for abnormal Pap smear results are beyond the scope of this synthesis. Refer to the guideline summary for additional recommendations on the following topics: • Screening Women with Special Circumstances • Recommended Management for Women with Abnormal Cytology

SCREENING MODALITY AND FREQUENCY

Abbreviations
Back to TOC

ACOG (2009)	***The following recommendations are based on good and consistent scientific evidence (Level A)***: • Cervical cytology screening is recommended every 2 years for women between the ages of 21 years and 29 years. • Women aged 30 years and older who have had three consecutive negative cervical cytology screening test results and who have no history of CIN 2 or CIN 3, are not HIV infected, are not immunocompromised, and were not exposed to diethylstilbestrol in utero may extend the interval between cervical cytology examinations to every 3 years. • Both liquid-based and conventional methods of cervical cytology are acceptable for screening. • Co-testing using the combination of cytology plus HPV DNA testing is an appropriate screening test for women older than 30 years. Any low-risk woman aged 30 years or older who receives negative test results on both cervical cytology screening and HPV DNA testing should be rescreened no sooner than 3 years subsequently. ***The following recommendations are based primarily on consensus and expert opinion (Level C)***: • Regardless of the frequency of cervical cytology screening, physicians also should inform their patients that annual

	gynecologic examinations may still be appropriate even if cervical cytology is not performed at each visit. **NGC Note**: This synthesis addresses screening in asymptomatic women at average risk of cervical cancer. Discussion of recommendations related to screening in women at increased risk and recommendations related to follow-up for abnormal Pap smear results are beyond the scope of this synthesis. Refer to the original guideline document for additional recommendations on screening in women at increased risk of cervical cancer.
KPCMI (2006)	**Recommendations: Effectiveness of Cervical Cancer Primary Screening Tests in Asymptomatic, Average-Risk Women** Either of the following tests are options for cervical cancer screening in asymptomatic, average-risk women under age 30. • Conventional cytology ***(Evidence-based: B)*** • Liquid-based cytology ***(Consensus-based)*** All of the following tests are acceptable options for cervical cancer screening in asymptomatic, average-risk women age 30 and older. • Conventional cytology ***(Evidence-based: B)*** • Conventional cytology and HPV testing*†** cytology ***(Consensus-based)*** • Liquid-based cytology ***(Consensus-based)*** • Liquid-based cytology and HPV testing*†** cytology ***(Consensus-based)*** **HPV testing has not been FDA approved as a standalone test for primary screening.* *†Combined cytology and HPV testing provides useful risk-stratification.* ***Hybrid Capture 2 (HC2) Testing Device.* No recommendation for or against routine use of computer-assisted slide evaluation or automated rescreening of cytology slides. ***(Evidence-based: I)*** **Recommendations: Cervical Cancer Screening Intervals in Asymptomatic, Average-risk Women** The following screening intervals are recommended: • Cytology alone: every 3 years* ***(Consensus-based)*** • Cytology + HPV (age 30 and older): every 3 years*† ***(Consensus-based)***

	Screen if more than 30 months has elapsed.* *†Hybrid Capture 2 (HC2) Testing Device.* No recommendation for or against routinely providing annual screening tests prior to beginning a triennial screening program. *(Evidence-based: I)*** **NGC Note**: This synthesis addresses screening in asymptomatic women at average risk of cervical cancer. Discussion of recommendations related to screening in women at increased risk and recommendations related to follow-up for abnormal Pap smear results are beyond the scope of this synthesis. Refer to the guideline summary for additional recommendations on the following topics: • Triage for ASC US Results Using HPV Testing in Asymptomatic, Average Risk Women • Screening in Women at Increased Risk of Cervical Cancer • Optimal Initial Management of Concurrent HPV Positive and Cytology Negative Cervical Screening Results

PEBC (2005)	**Optimal Cervical Screening Tool**
	
	• Liquid-based cytology is the preferred tool for cervical cytology screening (B-II). Conventional smear cytology remains an acceptable alternative (C-III).
	
	Screening Interval
	
	• Screening should be done annually until there are three consecutive negative Pap tests (C-III).
	• Screening should continue every two to three years after three annual negative Pap tests (B-II).
	  ◦ Screening at a three-year interval is recommended, supported by an adequate recall mechanism (B-II).
	  ◦ Women who have not been screened in more than five years should be screened annually until there are three consecutive negative Pap tests (C-III).
	
	NGC Note: This synthesis addresses screening in asymptomatic women at average risk of cervical cancer. Discussion of recommendations related to screening in women at increased risk and recommendations related to follow-up for abnormal Pap smear results are beyond the scope of this synthesis. Refer to the guideline summary for additional recommendations on the following topics:
	
	• Screening Women with Special Circumstances
	• Recommended Management for Women with Abnormal Cytology

ACOG (2009)	***The following recommendations are based on good and consistent scientific evidence (Level A)***: • In women who have had a total hysterectomy for benign indications and have no prior history of highgrade CIN, routine cytology testing should be discontinued. ***The following recommendations are based on limited and inconsistent scientific evidence (Level B)***: • Women who have had a hysterectomy with removal of the cervix and have a history of CIN 2 or CIN 3—or in whom a negative history cannot be documented—should continue to be screened even after their period of posttreatment surveillance. Whereas the screening interval may then be extended, there are no good data to support or refute discontinuing screening in this population.
KPCMI (2006)	**Recommendations: Optimal Cervical Cancer Screening Strategy for Women Who Have Had a Total Hysterectomy for a Benign Condition** Routine cytology screening is not recommended for women who have had a total hysterectomy for a benign condition unless there was a history of CIN grade 2/3. ***(Evidence-based: D)*** Three consecutive negative cytology results with or without HPV testing are recommended prior to discontinuation of screening in women who have a history of CIN grade 2/3 and a subsequent hysterectomy for a benign condition. ***(Consensus-based)***
PEBC (2005)	• Screening can be discontinued in women who have undergone total hysterectomy for benign causes with no history of cervical dysplasia or human papillomavirus (C-III). • Women who have undergone subtotal hysterectomy (with an intact cervix) should continue screening according to the guidelines.

STRENGTH OF EVIDENCE AND RECOMMENDATION GRADING SCHEMES Abbreviations Back to TOC	
ACOG (2009)	**Grades of Evidence**

I: Evidence obtained from at least one properly designed randomized controlled trial.

II-1: Evidence obtained from well-designed controlled trials without randomization.

II-2: Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.

II-3: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Levels of Evidence

Level A - Recommendations are based on good and consistent scientific evidence.

Level B - Recommendations are based on limited or inconsistent scientific evidence.

Level C - Recommendations are based primarily on consensus and expert opinion.

KPCMI (2006)

Recommendations are classified as either "evidence-based (A-D, I)" or "consensus-based."

- *Evidence-based*: sufficient number of high-quality studies from which to draw a conclusion, and the recommended practice is consistent with the findings of the evidence. A recommendation can also be considered "evidence-based" if there is insufficient evidence and no practice is recommended.
- *Consensus-based*: insufficient evidence and a practice is recommended based on the consensus or expert opinion of the Guideline Development Team.

Label and Language of Recommendations*

Label	Evidence-Based Recommendations
Evidence-based (A)	**Language**: [a] The intervention is strongly recommended for eligible patients. **Evidence**: The intervention improves important health outcomes, based on good evidence, and the Guideline Development Team (GDT) concludes that benefits

	substantially outweigh harms and costs. **Evidence Grade**: Good.
Evidence-based (B)	**Language**: [a] The intervention is recommended for eligible patients. **Evidence**: The intervention improves important health outcomes, based on 1) good evidence that benefits outweigh harms and costs; or 2) fair evidence that benefits substantially outweigh harms and costs. **Evidence Grade**: Good or Fair.
Evidence-based (C)	**Language**: [a] No recommendation for or against routine provision of the intervention. (At the discretion of the GDT, the recommendation may use the language "option," but must list all the equivalent options.) **Evidence**: Evidence is sufficient to determine the benefits, harms, and costs of an intervention, and there is at least fair evidence that the intervention improves important health outcomes. But the GDT concludes that the balance of the benefits, harms, and costs is too close to justify a general recommendation. **Evidence Grade**: Good or Fair.
Evidence-based (D)	**Language**: [a] Recommendation against routinely providing the intervention to eligible patients. **Evidence**: The GDT found at least fair evidence that the intervention is ineffective, or that harms or costs outweigh benefits. **Evidence Grade**: Good or Fair.
Evidence-based (I)	**Language**: [a] The evidence is insufficient to recommend for or against routinely providing the intervention. (At the discretion of the GDT, the recommendation may use the language "option," but must list all the equivalent options.) **Evidence**: Evidence that the intervention is effective is lacking, of poor quality, or conflicting and the balance of benefits, harms, and costs cannot be determined. **Evidence Grade**: Insufficient.
Consensus-based	**Language**: [a] The language of the recommendation is at the discretion of the GDT, subject to approval by the National Guideline Directors. **Evidence**: The level of evidence is assumed to be "Insufficient" unless otherwise stated. However, do not use the A, B, C, D, or I labels which are only intended to be used for evidence-based recommendations.

	Evidence Grade: Insufficient, unless otherwise stated.
	For the rare consensus-based recommendations which have "Good" or "Fair" evidence, the evidence must support a different recommendation, because if the evidence were good or fair, the recommendation would usually be evidence-based. In this kind of consensus-based recommendation, the evidence grade should point this out (e.g., "Evidence Grade: Good, supporting a different recommendation").

[a] All statements specify the population for which the recommendation is intended.

*Recommendations should be labeled and given an evidence grade. The evidence grade should appear in the rationale. Evidence is graded with respect to the degree it supports the specific clinical recommendation. For example, there may be good evidence that Drugs 1 and 2 are effective for Condition A, but no evidence that Drug 1 is more effective than Drug 2. If the recommendation is to use either Drug 1 or 2, the evidence is good. If the recommendation is to use Drug 1 in preference to Drug 2, the evidence is insufficient.

PEBC (2005)

Rating Scheme for the Strength of the Evidence

I. Evidence from at least 1 randomized controlled trial
II. Evidence from at least 1 clinical trial without randomization, from cohort or case-controlled analytic studies, or from multiple time series studies or dramatic results from uncontrolled experiments
III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

Rating Scheme for the Strength of the Recommendations

A. Good evidence for efficacy and substantial clinical benefit support recommendation for use.
B. Moderate evidence for efficacy or only limited clinical benefit support recommendation for use.
C. Evidence for efficacy is insufficient to support a recommendation for or against use, but recommendations may be made on other grounds.
D. Moderate evidence for lack of efficacy or for adverse outcome supports a recommendation against use.
E. Good evidence for lack of efficacy or for adverse outcome supports a recommendation against use.

COMPARISON OF METHODOLOGY

Click on the links below for details of guideline development methodology		
ACOG (2009)	**KPCMI (2006)**	**PEBC (2005)**
To collect and select the evidence all three groups performed searches of electronic databases. ACOG and PEBC also performed hand-searches of published literature (primary and secondary sources). All three guidelines provide details regarding the literature search, including the specific databases searched, time frames applied, and search terms used. All of the groups used weighting according to a rating scheme to assess the quality and strength of the evidence and all provide the scheme. Methods used to analyze the evidence were also similar, with all three groups performing a systematic review (the ACOG and KPCMI reviews incorporated evidence tables) and also performing a review of published meta-analyses. All of the groups employed expert consensus to formulate the recommendations, and all three graded them in strength according to a rating scheme. With regard to issues of cost, none of the groups performed a cost analysis. ACOG and KPCMI reviewed cost and analyses and studies. Internal peer review was utilized by all three groups as a method of validating the guideline and all provide a description of the validation process; PEBC also used external peer review by soliciting practitioner feedback through a mailed survey of 180 physicians.		

SOURCE(S) OF FUNDING Abbreviations Back to TOC	
ACOG (2009)	American College of Obstetricians and Gynecologists (ACOG)
KPCMI (2006)	Kaiser Permanente Care Management Institute
PEBC (2005)	Cancer Care Ontario Ontario Ministry of Health and Long-Term Care

BENEFITS AND HARMS Abbreviations Back to TOC
Benefits

ACOG (2009)	When cervical cytology screening programs have been introduced into communities, marked reductions in cervical cancer incidence have followed.
KPCMI (2006)	• Appropriate cervical cancer screening • Reduced morbidity and mortality from cervical cancer
PEBC (2005)	• Optimal use of cervical screening tools • Reduced incidence and mortality due to cervical cancer • Appropriate initiation, intervals, and cessation of cervical screening • Optimal management of women with abnormal cytology
Harms	
ACOG (2009)	• Mucosal atrophy common after menopause may predispose to false-positive cytology. False-positive results are likely to be followed with additional procedures, anxiety, and expense in this population. • In some cases, cervical cancer is undetected despite a recent screening test because of errors in sampling, interpretation, or follow-up.
KPCMI (2006)	• Inconvenience, anxiety, and adverse effects of tests (e.g., discomfort, pain, etc.) • Unnecessary tests due to false-positive test results • False reassurance from false-negative test results, neglect to follow-up, progression of cancer
PEBC (2005)	Not stated

Abbreviations
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ASC-US, atypical squamous cells of uncertain significance

ACOG, American College of Obstetricians and Gynecologists

CIN, cervical intraepithelial neoplasia

DNA, deoxyribonucleic acid

FDA, U.S. Food and Drug Administration

HIV, human immunodeficiency virus

HPV, human papillomavirus

KPCMI, Kaiser Permanente Care Management Institute

LBP, liquid-based Pap

Pap, Papanicolaou

PEBC, Program in Evidence-based Care

This synthesis was prepared by ECRI Insitute on September 1, 2005. The information was verified by UMHS on October 5, 2005, and by USPSTF on October 14, 2005. This synthesis was revised March 3, 2006 to include new recommendations from the Cancer Care Ontario Program in Evidence-based Care (PEBC). The updated information was verified by PEBC on April 5, 2006. The information was updated on October 26, 2007 to remove BWH recommendations and again on November 27, 2007 to remove recommendations from ACS. This synthesis was revised on January 27, 2008 to add KPCMI recommendations. The information was verified by KPCMI on February 22, 2008. This synthesis was updated in October 2008 to remove outdated USPSTF recommendations and again in January 2010 to add ACOG recommendations and remove outdated UMHS recommendations. The information was verified by ACOG on February 22, 2010.

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